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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/383,695 | 08/26/1999 | DAVID M. NEVILLE | 14014.0225 | 6915 |

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| EXAMINER | |
|---|---|
| UNGAR, SUSAN NMN | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1642 | 27 |

DATE MAILED: 10/21/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

| Application No. | Applicant(s) |
|---|---|
| 09/383,695 | Neville et al |
| **Examiner** | **Art Unit** |
| Ungar | 1642 |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1) ☒ Responsive to communication(s) filed on *Sep 16, 2002* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

**Disposition of Claims**

4) ☒ Claim(s) *1-4, 6, 9, 10, 22, and 26-29* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-4, 6, 9, 10, 22, and 26-29* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

**Application Papers**

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☑ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 23 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

1. The request filed on September 11, 2002 (Paper No. 25) for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 08/920,654 is acceptable and a CPA has been established. Further, the Amendment filed September 11, 2002 (Paper No. 26) is acknowledged and has been entered. Claims 1-4, 6, 9-10, 22, 26-29 are currently under prosecution. An action on the CPA follows.

2. The previously established priority date is maintained:

***Priority***

3. The priority date of April 15, 1997 previously established is maintained for the reasons previously set forth.

Applicant argues that to prove adequate written description in the provisional application, "[I]dentity of description is not necessary" and cites *New Railhead Mfg., L.L.C. v. Vermeer Mfg. Co* and further cites *Crown Operations Int'l Lts. V. Solutia Inc.*, wherein ["[T]he disclosure as originally filed does not have to provide in haec verba support for the claimed subject matter at issue."). Applicant further argues that Applicants must merely show that the same invention is described.

Applicant argues in particular as drawn to '104 that the specification at the cited pages describes the claimed invention. The argument has been considered but has not been found persuasive because a review of *New Railhead Mfg., L.L.C. v. Vermeer Mfg. Co* reveals that Applicant has neglected to cite the decision of the court wherein the court held that for a non provisional application to be afforded the priority date of the provisional application, "the specification of the provisional must 'contain a written description of the invention and the manner and process of

making and using it, in such full, clear, concise and exact terms,' 35 USC 112, first paragraph, to enable an ordinarily skilled artisan to practice the **claimed** invention in the non-provisional application. The court looked at claim 1 of the patent in question which recites a bit body being angled with respect to the sonde housing. The court then reviewed the provisional application and concluded that nowhere in the provisional application is the bit body expressly described as "being angled with respect to the sonde housing" as recited in claim 1 of the patent. The court held that the disclosure of the provisional application does not adequately support the invention claimed in the patent as to the angle limitation and therefore the patent is not entitled to the filing date of the provisional application under 35 USC 119(e)(1) and the patent in question was invalidated. Further, although it is clear that the instant disclosure does not have to provide in *haec verba* support for the claimed subject matter at issue, the disclosure must clearly convey possession of the claimed invention. A review of the cited support clearly reveals that none of the support cited is drawn to a method of inhibiting a rejection response in a primate comprising administering sFV-DT390 so as to reduce the recipient's T-cell lymphocyte population. Clearly, the instant situation is amenable to the type of analysis set forth in *New Railroad.* The provisional disclosure does not adequately support the invention claimed in the instant application as to the limitation of a method of inhibiting a rejection response in a primate comprising administering sFV-DT390 and therefore the application is not entitled to the filing date of the provisional ampliation under 35 USC 119(e). The provisional specification does not clearly convey that Applicant had possession of the claimed invention at the time, or even

contemplated the claimed invention at the time, the provisional application was filed.

Applicant argues in particular as drawn to '459 that the specification at the cited pages describes the claimed invention. The argument has been considered but has not been found persuasive because a review of the cited support clearly reveals that none of the support cited is drawn to a method of inhibiting a rejection response in a primate comprising administering sFV-DT390 so as to reduce the recipient's T-cell lymphocyte population. Clearly, the instant situation is amenable to the type of analysis set forth in *New Railroad.* The provisional disclosure does not adequately support the invention claimed in the instant application as to the limitation of a method of inhibiting a rejection response in a primate comprising administering sFV-DT390 and therefore the application is not entitled to the filing date of the provisional ampliation under 35 USC 119(e). The provisional specification does not clearly convey that Applicant had possession of the claimed invention at the time, or even contemplated the claimed invention at the time, the provisional application was filed.

Applicant further argues in particular as drawn to '703 that the specification at the cited pages describes the claimed invention. The argument has been considered but has not been found persuasive because a review of the cited support clearly reveals that none of the support cited is drawn to a method of inhibiting a rejection response in a primate comprising administering sFV-DT390 so as to reduce the recipient's T-cell lymphocyte population prior to administration of the immunotoxin. Clearly, the instant fact pattern, although drawn to a non-provisional

parent application; is amenable to the type of analysis set forth in *New Railroad.* The relied upon disclosure does not adequately support the invention claimed in the instant application as to the limitation of a method of inhibiting a rejection response in a primate comprising administering sFV-DT390 and therefore the claimed invention is not entitled to the filing date of the parent non-provisional application. The relied upon specification does not clearly convey that Applicant had possession of the claimed invention at the time, or even contemplated the claimed invention at the time, the provisional application was filed. Applicant's arguments have not been found persuasive and the establishment of the priority date is maintained.

4. The following rejections are maintained:

***Double Patenting***

5. Claims 1-4, 6, 9-10 and 22 remain rejected under nonstatutory double patenting for the reasons previously set forth in Paper No. 13, Section 8, pages 5-8 and in Paper No.20, Section 8, pages 5-6.

Applicant argues that the double patenting rejection is overcome as the application is entitled to the priority date of October 30, 1995 which antedates the Thomas reference from November 24, 1995 and the '235 patent filed April 15, 1995.

The argument has been considered but has not been found persuasive because the application is not entitled to the priority date of October 30, 1995 for the reasons set forth previously and above. Applicant's arguments have not been found persuasive and the rejection is maintained is maintained.

***Claim Rejections - 35 USC § 103***

6. Claims 1-4, 6, 9-10, 22, 26-29 remain rejected under 35 USC 103 for the reasons previously set forth in Paper No. 20, Section 9, page 6 and for the reasons recited in the Papers and sections cited therein.

Applicant argues that the rejection under 35 USC 103 is overcome as the application is entitled to the priority date of October 30, 1995 which antedates the Thomas reference from November 24, 1995 and the '235 patent filed April 15, 1995.

The argument has been considered but has not been found persuasive because the application is not entitled to the priority date of October 30, 1995 for the reasons set forth previously and above. Applicant's arguments have not been found persuasive and the rejection is maintained is maintained.

***New Grounds of Objection***

7. The amendment filed September 11, 2002 (Paper No. 26) is objected to under 35 U.S.C. § 132 because it introduces new matter into the specification. 35 U.S.C. § 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is the incorporation by reference of the parent applications of the instant application. MPEP 201.06(c) specifically states that:

> A priority claim under 35 U.S.C. 120 in a continuation or divisional application does not amount to an incorporation by reference of the application(s) to which priority is claimed. For the incorporation by reference to be effective as a proper safeguard against the omission of a portion of a prior application, the incorporation by reference statement must be included in the specification-as-filed, or transmittal letter-as-filed, or in an amendment specifically referred to in an oath or declaration executing the application.

> Mere reference to another application, patent, or publication is not an incorporation of anything therein into the application containing such reference for the purpose of the disclosure required by 35 U.S.C. 112, first paragraph. In re de Seversky, 474 F.2d 671, 177 USPQ 144 (CCPA 1973). See MPEP § 608.01(p).

Applicant is required to cancel the new matter in the response to this Office action.

***New Grounds of Rejection***

***Claim Rejections - 35 USC § 112***

8. Claims 26-29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of inhibiting a rejection response in a non-human primate recipient by inducing immune tolerance to foreign mammalian donor cells, does not reasonably provide enablement for a method of inhibiting a rejection response in a primate recipient by inducing immune tolerance to foreign mammalian donor cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The claims are drawn to a method of inhibiting a rejection response in a primate recipient by inducing immune tolerance to foreign mammalian donor cells. This includes all types of primates, human primates. It is noted that Auchincloss (chapter 11 in Transplantation Immunology, Bach and Auchincloss Eds. Wiley-Liss, New York, 1995, pages 211-218), of record, specifically teaches that tolerance is the long-lasting nonreactivity of the immune system to a specific set of antigens, maintained without on-going immunosuppression, see page 211. The specification

teaches that transplant tolerance in humans remains an elusive goal and physicians would like to see successful, allogeneic organ transplant without the necessity for indefinite non-specific maintenance with immunosuppressive drugs (p. 2) and teaches that the present invention meets the need by providing a method of inducing immune tolerance (p. 3). The specification teaches a method of inducing immune tolerance by administering an immunotoxin to reduce recipient's peripheral blood T-cell lymphocyte population by at least 80% (p. 17) and teaches that the method can further include administering corticosteroids, donor leukocytes, immunosuppressants (p. 18). The specification exemplifies the survival of allografted monkeys with CD3 immunotoxin alone wherein they survived 51-79 days (page 97), 51, >165 days (page 84) with extended survival for those animals that had additional immunosuppressive treatment (page 84) and specifically teaches that following depletion, complete T-cell recovery occurs in three to four weeks (page 82). One cannot extrapolate the teaching of the specification to the scope of the claims because it is clear that although it appears that immune tolerance may be achieved in some of the rhesus monkeys used, it is not clear that this finding can be extrapolated to the development of immune tolerance in humans. The specification, in agreement with Auchincloss, clearly teaches that "immune tolerance" is meant to be tolerance that allows transplant recipients to go without the necessity for indefinite non-specific maintenance with immunosuppressive drugs (see page 2). However, the unpredictability of the art is exemplified by both Auchincloss, *Supra,* Monaco (Immunomethods, 1993, 2:159-170), of record and Wee et al (Transplantation, 1994, 58:261-264), of record. Auchincloss teaches, at the

Conclusion on page 217, that although more than a dozen different techniques to induce tolerance in rodents are now available, the fact remains that none of them has been used successfully in the clinic. Neither the specification nor the art of record has provided evidence that human tolerance to graft in humans has been successfully achieved. It is noted that a review of the literature has not produced evidence of the successful achievement of immune tolerance to graft in humans. Thus, the induction of immune tolerance to graft in humans is an undeveloped art. As Auchincloss teaches, inducing transplantation tolerance in humans must be very hard to do, thus those reading the chapter should be wary of simple solutions to this complex process. Monaco, of record discloses that the induction of specific tolerance to tissue allografts and xenografts continues to be a subject of intense experimentation, however significant problems remain (see Abstract). In reviewing the experimental evidence, Monaco points out the species and model dependency of achieving transplantation tolerance (see entire document). Further, Wee et al. disclose the art-known experience that permanent allograft acceptance has not been achieved in any of the large animal models (first paragraph) and the permanent allograft acceptance is much more difficult to induce in higher animals that in previously reported rodent models (last paragraph) (Transplantation, 1994). Based on the information in the art and the statements in the specification drawn to the elusiveness of the goal of transplant tolerance, it could not be predicted that the invention would function as claimed in human primates. In view of the lack of predictability of the art to which the invention pertains the lack of established clinical protocols for effective tolerance-induction therapies, undue experimentation

would be required to practice the claimed method in human primates with a reasonable expectation of success .

Applicant is invited to consider alternative therapeutic endpoints for human primates such as immunosuppression in contrast to the claimed therapeutic endpoint of tolerance.

Applicants arguments drawn to the previous rejection of claims 26-29 are relevant to the instant rejection.

Applicant argues that (a) Thomas et al (Transplantation 2000, 69, 2497-2508) provides enablement for the claimed invention, (b) Table 7, p. 97, and p. 87 provide enablement for the claimed invention.

The arguments have been considered but has not been found persuasive because (a') the claimed invention, as broadly constituted is drawn to induction of immune tolerance to graft in human primates. The Thomas et al reference is not commensurate in scope with the claimed invention, (b") neither Table 7 nor page 97 nor p. 87 are commensurate in scope with the broadly claimed invention.

9. No claims allowed

10. All other objections and rejections recited in Paper No. 20 are withdrawn.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Ungar, PhD whose telephone number is (703) 305-2181. The examiner can normally be reached on Monday through Friday from 7:30am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached at (703) 308-3995. The fax phone number for this Art Unit is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Effective, February 7, 1998, the Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1642.

Susan Ungar
Primary Patent Examiner
October 17, 2002